REMARKS

The present invention is directed to methods and compositions for the treatment of cancer comprising the administration of neuraminidase. In particular, the present invention is directed to methods and compositions for treating cancer wherein the effective dosage amount of the neuraminidase is extremely low. Claims 1, 2, 4-9 and 13-17 are pending. The Applicant would like to thank the Examiner for withdrawing the rejection under 35 U.S.C. § 112.

Rejection under 35 U.S.C. §103

In the December 1, 2004 Office Action, claims 1, 2, 4-9 and 13-17 were rejected under 35 U.S.C. §103(a) as being obvious over Sedlacek et al. 1986, *Cancer Immunol Immunother* 23:192-199 ("Sedlacek '86") or Sedlacek et al. 1987, *Int J Immunopharmac* 9(7): 841-850 ("Sedlacek '87") in view of U.S. Patent No.5,736,133 ("Kline '133") or U.S. Patent No.5,558,863 ("Kline '863") and U.S. Patent No. 3,792,159 ("Green") Applicant respectfully traverses this rejection.

The Examiner asserts that the Sedlacek references disclose the use of neuraminidase to treat cancer and that the Kline references disclose the amounts of neuraminidase to use along with the methods of administration. Furthermore the Examiner asserts that Green discloses the use of phenol saline as a carrier and that these references disclose the claimed method when taken as a whole. The Examiner maintains that it would be obvious for the skilled artisan to prescribe multiple doses of neuraminidase although the cited art fails to teach such administration.

Both Kline '133 and '863 disclose the claimed dosage range of 10^{-2} to 10^{-8} mg for the treatment of *viral infections*, not for the treatment of *cancer*. As such, the Kline patents are non-analogous art and one of ordinary skill in the art would not be motivated to use either Kline '133 or '863 for disclosure of an effective dosage of neuraminidase to treat cancer. There is no motivation to combine the teachings of either of these patents with Sedlacek for the treatment of cancer.

Green discloses processes for preparing injectable compositions. Specifically, Green discloses washing and resuspending a composition of tyrosine and an allergen in phenol saline. Unlike the present invention, Green fails to disclose suspending of neuraminidase in phenol saline, and also fails to disclose treating cancer with such a composition.

Both Sedlacek '86 and '87 disclose vaccinating an animal with tumor cells treated with neuraminidase. Vaccination is not the same as providing a treatment regime for cancer. Furthermore, as would be apparent to one skilled in the art, "preventive medicine" and "treatment medicine" are not routinely equivalent or analogous. Unlike the present invention, Sedlacek does not disclose administering multiple doses of a low amount of neuraminidase per day to a patient. While the Examiner asserts that a physician would know to prescribe multiple doses to treat cancer, the prior art fails to teach this method. The Examiner also implies a "more is better" method in the aggressive treatment of cancer. While multiple dosing is part of the Kline application, the relevance is in the *extremely low amount of neuraminidase per dose.* More is not better in this case. Furthermore, uninterrupted continuous use of neuraminidase has deleterious, not beneficial side effects. For example, a case study reported to the Applicant described a patient with aggressive, stage 4 liver cancer who initiated neuraminidase treatment at a 29% increase over the low dosage amount taught by the specification and developed critical levels of jaundice and inflammation of the liver. Side effects stopped with cessation of the treatment and did not reoccur when treatment continued at the appropriate low doses. Applicants offer to submit a Declaration under 37 C.F.R. 1.132 containing this report should the Examiner require it.

The Examiner also asserts that the Sedlacek method was an "experiment in one shot to see the effects of the neuraminidase" and it would be obvious to increase administration to multiple doses. If this assertion were true, there would only be *one* article reporting these findings. The fact that both Sedlacek articles use the same method confirms the "one shot" format of the vaccination method and that multiple administrations are not contemplated or taught by either references. *Both* articles by Sedlacek disclose *single* administrations of

neuraminidase with tumor cells for *vaccination*. The presence of a second article on this method, without further experiments using multiple per day doses, indicates that the method of Sedlacek is intended for "one shot" format only. The Sedlacek method is clearly different from the claimed method. A physician would not be motivated to administer a neuraminidase composition more than once in view of *both* Sedlacek articles disclosing only a *single* chessboard vaccination event. Absent the teachings of the present specification and the examples showing the efficacy of a multiple per day treatment regime, one of ordinary skill in the art would not arrive at the claimed method based on the teachings of the Sedlacek references individually or in combination with the other cited references.

There are secondary considerations that must also be evaluated when maintaining a rejection of obviousness. Such considerations include long-felt need and failure of others, and skepticism of experts. The remarkable silence in the art regarding use of neuraminidase to treat cancer since 1987 and 1988, when the Sedlacek articles were published, gives further support to the non-obviousness of the claimed method. Thousands of people die each year from cancer and the public outcry from these deaths has increased the amount of government funding to cancer research and motivated pharmaceutical companies to develop other cancer treatments. In the 15 years since the Sedlacek articles were published, there has been no further report of using neuraminidase to treat cancer. In light of this profound gap in the evolution of this research, there can be no valid assertion that the claimed method is obvious or else it would have been pursued much sooner than in the present application.

Furthermore, the skepticism of experts also provides evidence of the non-obviousness of an invention. The Examiner himself displayed skepticism in the form of a §112 enablement rejection which was successfully overcome in view of the data presented in the Examples of the specification. The Applicant has succeeded in treating cancer where others have failed. Skepticism would not have been present were the claimed method truly obvious. In view of the foregoing comments, The Applicant respectfully requests withdrawal of this rejection.

Conclusion

The Applicant submits that the pending claims define novel and patentable subject matter and provide a complete response to the Office Action. Accordingly, the Applicant respectfully request allowance of these claims. No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required, or credit any overpayment, to Deposit Account Number 11-0855.

If the Examiner believes any informalities remain in the application that can be resolved by telephone interview, a telephone call to the undersigned attorney is earnestly solicited.

Allowance of claims 1, 2, 4-9 and 13-17 is respectfully solicited.

Respectfully submitted,

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